Tetrahedron Letters 52 (2011) 1363–1367

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

# Recycling of osmium catalyst in oxidative olefin cleavage: a chemoentrapment approach

Seyoung Kim, Jooyoung Chung, B. Moon Kim *

*Department of Chemistry, College of Natural Sciences, Seoul National University, Seoul 151-747, South Korea*

ARTICLE INFO

*Article history:*
Available online 20 January 2011

*Keywords:*
Catalyst recycle
Osmium tetroxide
Lemieux–Johnson
Chemoentrapment
Olefin cleavage

ABSTRACT

A new chemoentrapment strategy for recycling osmium in the catalytic olefin cleavage reaction is reported. The new strategy utilizes KOH/*i*-PrOH to generate water-soluble Os(VI) species as a recyclable metal catalyst after the oxidative cleavage reaction. For the recycling of the catalyst, $NaIO_4$–$NaClO_2$ was found to be the best combination of secondary oxidants and acetonitrile–water was chosen as an optimal solvent for the best recycling results. The new method allows for an efficient recycling of osmium in the reactions involving mono- and di-substituted olefins with 1 mol % of $OsO_4$ without any significant side reactions and loss of yield.

Oxidative cleavage of olefins to aldehydes and/or ketones is one of the many useful tools in the arsenal of organic chemists. Ozonolysis is one of the standard methods for the oxidative cleavage of olefins in laboratories; however, the use of ozone may raise safety concerns especially in the case of large scale applications. In ozonolysis, olefin turns into ozonide and can directly be transformed to aldehydes/ketones, alcohols, or carboxylic acids depending upon workup conditions.[1] On the other hand, Lemieux–Johnson (L–J) reaction and its variants are used for the oxidative cleavage of 1,2-diols and olefins. Although very useful, these reactions often require quite expensive metal catalysts, such as osmium or ruthenium. Therefore, cleavage of olefins employing $OsO_4$/$NaIO_4$ does not typically represent a practical reaction on a large scale. In this regard, the development of efficient ways to minimize or recycle the use of expensive metal catalysts is of much interest to organic chemists. So far, various methods for the reuse of osmium catalyst have been developed mostly in the context of dihydroxylation. For example, microencapsulation of $OsO_4$ in a polymer matrix,[2] fixation of osmium onto olefins covalently bound on silica support,[3] use of ion-exchange supports,[4] use of an ionic liquid to immobilize osmium species,[5] and supportless chemoentrapment approach developed in our laboratory[6] have been reported. To the best of our knowledge, there is one report on osmium recycling in Lemieux–Johnson type olefin cleavage reaction, which employed microencapsulated osmium tetroxide.[7] However, in this method, extra preparation step of osmium polyurea microcapsules was required, and reactions using this microencapsulated osmium species proceeded in lower yields than those using homogeneous osmium catalysts. Therefore, we focused our attention to the development of a new practical recycling method of osmium catalyst for the L–J reaction.

To gain insights on how we could find efficient ways to recycle osmium in L–J reaction, we examined osmium recycling in the dihydroxylation reaction. In the case of typical asymmetric dihydroxylation (AD) reaction employing $K_3Fe(CN)_6$ as a secondary oxidant, after the reaction with an olefin, osmium catalyst is converted to an osmate(VI) ester. Then it is oxidized by the secondary oxidant to an Os(VIII) species and hydrolyzed, and migrates back to the organic phase to repeat the cycle.[8] To chemically trap all of the osmium species as water-soluble Os(VI), it is essential to block the oxidation of Os(VI) to Os(VIII) in the aqueous layer. In other words, conversion of the remaining oxidant with a trapping agent, which is an extra reductant, is necessary. We previously reported the use of ethyl vinyl ether (EVE) as a trapping reagent for the quenching of the extra oxidant in catalytic AD.[6] Since most of the L–J type reactions are carried out using an organic/aqueous biphasic solution,[9] EVE treatment was expected to work in a similar way in L–J reactions as shown in a schematic diagram of osmium recycling in Figure 1.

First we examined the previously developed chemoentrapment method employing EVE for the recycling of Os in the L–J reaction.[6] A series of test reactions were run using 0.5 mol % of $OsO_4$ in the presence of $NaIO_4$ (260 mol %) per 100 mol % substrate in *tert*-BuOH and water. After each reaction cycle, 1.0 equiv EVE was added to the reaction mixture. Then all organic compounds were extracted using *tert*-butyl methyl ether (TBME). The recovered aqueous layer was reused for the next reaction after adding a new batch of $NaIO_4$ and *tert*-BuOH and the results are shown in Table 1. When there was no treatment with EVE, the reaction yield

---

* Corresponding author. Tel.: +82 2 880 6644; fax: +82 2 872 7505.
*E-mail address:* kimbm@snu.ac.kr (B.M. Kim).

0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.01.065

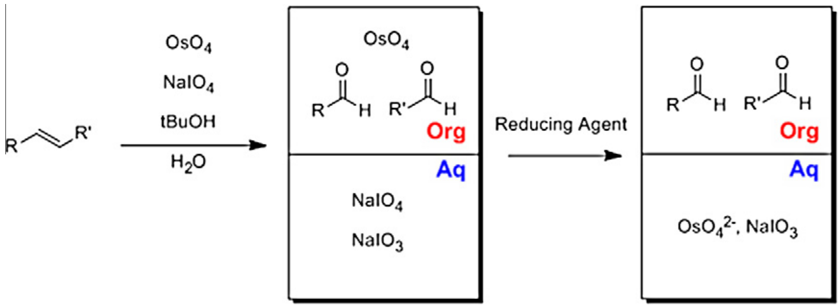
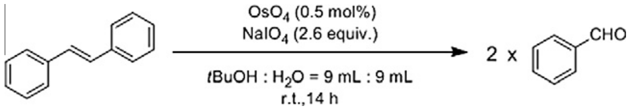


**Figure 1.** A schematic diagram of osmium recycling using a chemoentrapment approach.

**Table 1**
Ttrial of osmium recycle using EVE and IPA–KOH combination



| Entry | Treat | Conversion[a,b] (%) | | | | |
|---|---|---|---|---|---|---|
| | | 1st | 2nd | 3rd | 4th | 5th |
| 1 | None | 99 | 9 | 2 | — | — |
| 2 | EVE | 99 | 40 | 36 | 26 | 30 |
| 3 | IPA | 99 | 36 | 3 | | |
| 4 | IPA–KOH | 99 | 97 (19) | 99 (19) | 93 (44) | 98 (41) |

[a] All conversions were determined by HPLC analysis with mesitylene as an internal standard.

[b] Values in parentheses are yields of diol.

precipitously dropped to 9% at the second reaction (entry 1). As shown in entry 2, however, recycling reactions after EVE treatment provided sustained reactivity although quite low yields were observed even from the second reaction. We envisioned that EVE may be the culprit for the poor conversion in this case. Although it serves well for the reduction of the secondary oxidant and Os(VIII) in the case of dihydroxylation, the cleavage products of EVE in the L–J reaction (ethyl formate and formaldehyde) remaining in the aqueous layer can be further oxidized under the reaction conditions, causing premature depletion of the oxidant in the next step and the accumulation of oxidation product(s) in the aqueous layer.

In search for a more suitable reducing agent, we set the criteria required for a successful recycling of catalyst in L–J reaction: (1) efficient and simple oxidation step (no further oxidation of the trapping agent); (2) after the olefin cleavage, efficient reduction of $OsO_4$ and $NaIO_4$; (3) after the trapping of the catalyst in the aqueous layer, easy separation of the product from the reaction mixture. While searching for a reagent which would satisfy the above criteria, we found that isopropyl alcohol (IPA) is easily oxidized to acetone using a catalytic amount of osmium tetroxide in the presence of potassium hydroxide,[10] thus IPA–KOH can be a potential reducing system for Os(VIII) species. We then decided to apply this IPA–KOH system toward osmium recycling in L–J reaction. First it was confirmed that IPA alone was not effective in the recycling of the catalyst (entry 3). When IPA and KOH (150 mol % each) were added to the reaction mixture after the complete oxidation of olefin, it was successful to trap the reduced osmium catalyst in the aqueous layer. When this reducing system was applied to recycling experiments, it was effective until the fifth cycle, and *trans*-stilbene was completely converted to oxidized products (entry 4).

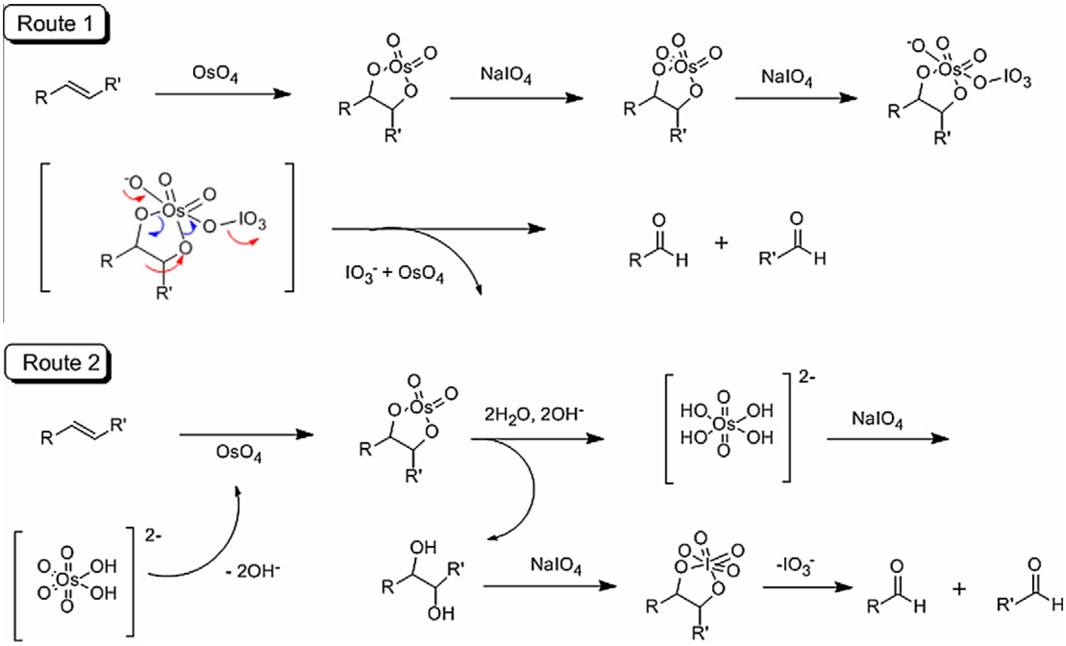
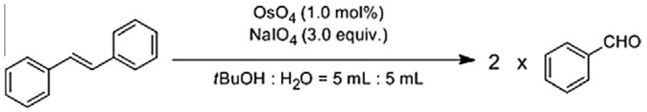


**Figure 2.** Proposed mechanism of two different routes of olefin cleavage mediated by $OsO_4$ and $NaIO_4$ depending upon the reaction conditions.

**Table 2**
Result of olefin cleavage with various treatment conditions



| Entry | Treatment | Neutralization | Conversion[a,b] (%) | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | 1st | 2nd | 3rd | 4th | 5th | 6th |
| 1 | IPA–KOH | No | 99 | 97 | 96 (20) | 99 (72) | 98 (40) | 98 (72) |
| 2 | IPA–KOH | Yes | 99 | 99 | 99 | 99 | 99 | 99 |

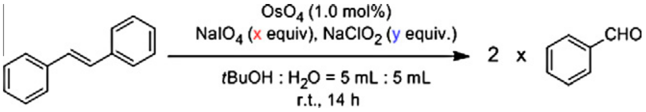
[a] All conversions were determined by HPLC analysis with mesitylene as an internal standard.
[b] Values in parentheses are yields of diol.

As seen in Table 1, IPA–KOH system proved to be a suitable reducing agent and the osmium catalyst was efficiently preserved in aqueous phase, availing itself for the next recycling step. However, under the IPA–KOH conditions, oxidation of *trans*-stilbene produced not only benzaldehyde but also a considerable amount of stilbenediol (entry 4, Table 1). We assumed that the byproduct formation is due to the remaining potassium hydroxide in the aqueous layer. From the mechanistic point of view outlined in Figure 2, under neutral conditions olefin oxidation may proceed via route 1 to give clean cleavage products. On the other hand, under basic conditions, the cyclic osmate is hydrolyzed generating 1,2-diol species and diol cleavage with $NaIO_4$ becomes slow under basic conditions (route 2). Therefore, the overall reaction rate will be slower than that of one-step route under neutral conditions and in the basic system, the remaining diol is identified after the reaction.[11] From these results, we concluded that securing a neutral condition is essential for the clean olefin cleavage reaction. To neutralize the aqeous layer after treatment with IPA–KOH followed by extraction of organic material with TBME, 1 N aq HCl solution was added to adjust the reaction mixture pH to 6–7. Then a new reaction was commenced with new batches of *trans*-stilbene, $NaIO_4$, and *tert*-BuOH. As a result of this treatment, we obtained benzaldehyde with excellent yields until the 6th cycle without a significant decrease of reactivity or formation of side products (entry 2, Table 2), which contrasts drastically with the results of non-neutralized reaction conditions (entry 1, Table 2).

During the recylcing of the osmium catalyst, accumulation of sodium iodate is a common problem during the recycling reactions. Although sodium periodate and iodate have relatively good solubility in water (80–90 g/l), increased precipitation of inorgaic salts resulted in difficult magnetic stirring. Dilution of the thick aqueous phase with additional water can make the stirring better, however, a fundamental solution is needed. Therefore, we set out to find a highly soluble secondary oxidant, which can lessen the accumulation of salt in aqueous layer.

As an oxidative reagent, sodium chlorite ($NaClO_2$) is utilized in many oxidative reactions, such as epoxidation,[12] dihydroxylation of olefins,[13] oxidation of sulfides to sulfoxides,[14] and primary alcohols to the carboxylic acids.[15] After oxidation, it generates highly water soluble NaCl and, to our delight, can also regenerate periodate from iodate.[16] To find the optimal reaction conditions, combinations varying the amounts of sodium chlorite and sodium periodate were examined and the results are listed in Table 3. In the absence of $NaIO_4$, formation of significant amount of aldehydes was not observed and stilbenediol was the major product independent of the amount of $NaClO_2$ used (entries 1–4). When the ratio of $NaClO_2$ to $NaIO_4$ is large (entries 3–6), oxidation did not go to completion but stopped at the stilbenediol stage. Although $NaClO_2$ is capable of regenerating $NaIO_4$, in this oxidant system, incomplete oxidation at the diol stage is evident due to a relatively low

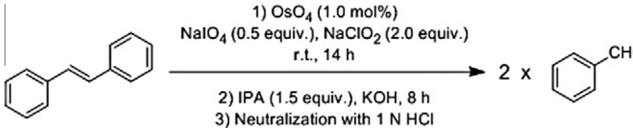
**Table 3**
Combination screening to find optimal oxidant combination



| Entry | Amount of oxidant (equiv) | | Conversion[a,b] (%) |
|---|---|---|---|
| | $NaIO_4$ | $NaClO_2$ | |
| 1 | 0 | 1.0 | 70 (8) |
| 2 | 0 | 2.0 | 95 (24) |
| 3 | 0 | 3.0 | 95 (24) |
| 4 | 0 | 4.0 | 98 (21) |
| 5 | 0.25 | 1.0 | 67 |
| 6 | 0.25 | 2.0 | 76 |
| 7 | 0.25 | 3.0 | 92 (84) |
| 8 | 0.25 | 4.0 | 98 (67) |
| 9 | 0.5 | 1.0 | 84 |
| **10** | **0.5** | **2.0** | **97** |
| 11 | 0.5 | 3.0 | 97 |
| 12 | 0.5 | 4.0 | 98 |
| 13 | 1.0 | 1.0 | 98 |
| 14 | 1.0 | 2.0 | 94 |
| 15 | 1.0 | 3.0 | 95 |
| 16 | 1.0 | 4.0 | 99 |

[a] All conversions were determined from HPLC analysis using mesitylene as an internal standard.
[b] Values in parentheses are yields of diol.

**Table 4**
Recycling of olefin cleavage in various solvents



| Entry | Solvent | Conversion[a,b] (%) | | | | | |
|---|---|---|---|---|---|---|---|
| | | 1st | 2nd | 3rd | 4th | 5th | 6th |
| 1 | *t*BuOH/$H_2O$<br>(1:1) | 95<br>(21) | 99<br>(33) | 97<br>(36) | 96<br>(27) | 99<br>(81) | 9<br>(0) |
| 2 | Dioxane/$H_2O$<br>(1:1) | 99 | 97 | 84<br>(18) | 93<br>(15) | 98<br>(16) | 79<br>(5) |
| 3 | THF/$H_2O$<br>(1:1) | 99<br>(22) | 99<br>(27) | 99<br>(39) | 99<br>(20) | 99<br>(27) | 99<br>(22) |
| 4 | MeCN/$H_2O$<br>(1:1) | 99 | 99 | 93 | 99 | 99 | 98 |
| 5 | $H_2O$/MeCN/<br>$CCl_4$ (3:2:2) | 99<br>(89) | 86<br>(68) | 99<br>(46) | 58<br>(48) | 18<br>(0) | 27<br>(0) |
| 6 | $H_2O$ only | 6 | 1 | 0 | 4 | 1 | 1 |

[a] All conversions were determined by HPLC analysis with mesitylene as an internal standard.
[b] Values in parentheses are yields of diol.

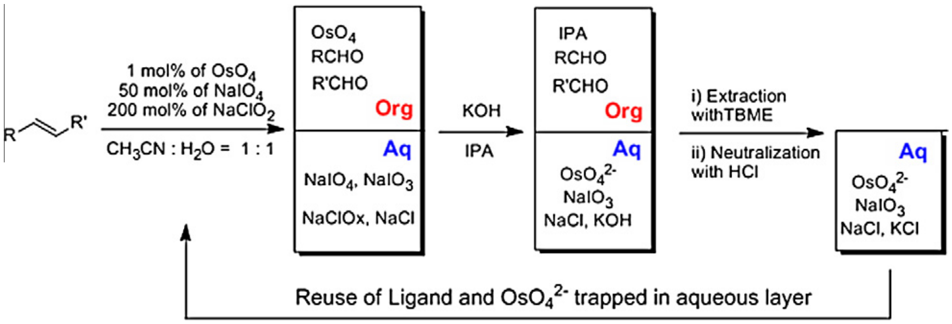
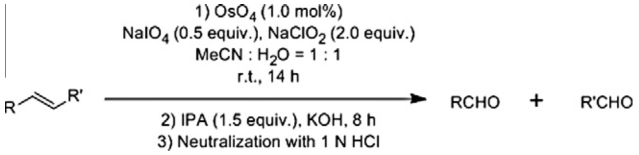


**Figure 3.** Schematic diagram of recycling of osmium catalyst using IPA as a reducing agent.

**Table 5**

Substrate scope under the optimal recycling conditions



| Entry | Olefin | Yield[a] (%) | | | | | |
|---|---|---|---|---|---|---|---|
| | | 1st | 2nd | 3rd | 4th | 5th | 6th |
| 1 | *trans*-Stilbene | 99 | 99 | 93 | 99 | 99 | 98 |
| 2 | Styrene[b] | 99 | 99 | 99 | 99 | 99 | 78 |
| 3 | α-Methylstyrene | 77 | 50 | 27 | 40 | 57 | 42 |
| 4 | *trans*-β-Methyl-styrene | 99 | 98 | 98 | 86 | 92 | 88 |
| 5 | Allyloxybenzene | 99 | 99 | 88 | 85 | 74 | 66 |
| 6 | Allylbenzene | 55 | 90 | 75 | 75 | 65 | 47 |
| 7 | 1-Phenyl cyclohexene | 74 | 47 | 42 | 41 | 39 | 26 |
| 8 | Cyclohexene | 40 | 70 | 70 | 67 | 61 | 51 |
| 9 | Norbonylene | 40 | 51 | 48 | 43 | 19 | 23 |

[a] Yields of isolated products.

[b] Yields were determined with HPLC integration with mesitylene as the internal standard.

concentration of $NaIO_4$. It was observed that at least 0.5 equiv of $NaIO_4$ is needed to produce aldehyde in high yields, and no increase of yield was observed even with excess $NaClO_2$ (entries 9–12). Therefore, we chose a combinaiton of 0.5 equiv of $NaIO_4$ and 2 equiv of $NaClO_2$ (entry 10) for optimal olefin cleavage conditions in *t*-BuOH and water.

With the optimal combination of $NaIO_4$ and $NaClO_2$ for an oxidant pair, we applied the reaction conditions to recycling experiments in *tert*-BuOH/$H_2O$ system with IPA–KOH protocol. Oxidation judged by the disappearance of stilbene was maintained upon recycling, however, yield of benzaldehyde decreased noticeably from the second cycle leaving some diol products (Table 4, entry 1), which may be due to slow oxidation rate. In order to speed up the oxidation, we invesitagted the influence of solvents on the reactivity. In the case of aqueous *t*-BuOH, THF or dioxane system, although stilbene disappeared completely in 14 h until the 6th cycle, products in each cycle contained about 20% of diol (entries 1–3). We then examined various solvent–water combinations and found that reaction in acetonitrile–water pair exhibited the most optimal reactivity showing clean oxidation to aldehydes in 14 h upto the 6th recycle (entry 4). The tri-solvent system, $CCl_4$–$CH_3CN$–water often employed in ruthenium-mediated oxidation[17] provided no significant advantage over the $CH_3CN$–water system (entry 5). When the reaction was run in water only, only a minimal amount of oxidation product was formed (entry 6).

A diagram showing the recycling process using all the optimized reaction conditions is shown in Figure 3.

Finally, to test the substrate scope of the optimal recycling conditions, a repetitive oxidative cleavage of various olefins was run with recycled catalyst upto six times and the results are shown in Table 5[18] Oxidation of *trans*-stilbene, styrene, and *trans*-β-methylstyrene proceeded smoothly to provide aldehydes upon the 6th recycling (entries 1, 2, and 4). However, recycling reactions of α-methylstyrene, allyloxybenzene, and allylbenzene showed somewhat decreased yields upon recycling (entries 3, 5, and 6). With cyclic olefins, such as cyclohexene, 1-phenylcyclohexene, and norbonene, desired aldehydes were obtained in only moderate yields (entries 7–9). The low yields of aldehydes in these cases are presumably due to slow conversion of diols to aldehydes.

In summary, we have developed a new chemoentrapment strategy for recycling osmium in the catalytic olefin cleavage reaction. IPA–KOH treated aqueous layer was able to successfully trap osmium catalyst as a water soluble form, and allowed for an efficient recycling of osmium in the oxidative cleavage reactions of olefins with 1 mol % of $OsO_4$ without any significant side reactions in good yields. Among several solvent systems examined, acetonitrile–water pair worked the best for efficient recycling reactions. Mono- and di-substituted olefins are the best substrates for this recyclable oxidative cleavage.

## Acknowledgment

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2009-0073645).

## References and notes

1. Travis, B. R.; Narayan, R. S.; Borhan, B. *J. Am. Chem. Soc.* **2002**, *124*, 3824.
2. (a) Kobayashi, S.; Endo, M.; Nagayama, S. *J. Am. Chem. Soc.* **1999**, *121*, 11229; (b) Kobayashi, S.; Ishida, T.; Akiyama, R. *Org. Lett.* **2001**, *3*, 2649; (c) Ley, S. V.; Ramarao, C.; Lee, A.; Østergaard, N.; Smith, S. C.; Shirley, I. M. *Org. Lett.* **2003**, *5*, 185; (d) Ishida, T.; Akiyama, R.; Kobayashi, S. *Adv. Synth. Catal.* **2003**, *345*, 576; (e) Ishida, T.; Akiyama, R.; Kobayashi, S. *Adv. Synth. Catal.* **2005**, *347*, 1189.
3. (a) Sevreyns, A.; De Vos, D. E.; Fiermans, L.; Verpoort, F.; Grobet, P. G.; Jacobs, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 586; (b) Yang, J. W.; Han, H.; Roh, E. J.; Lee, S. G.; Song, C. E. *Org. Lett.* **2002**, *4*, 4685.
4. (a) Choudary, B. M.; Chowdari, N. S.; Kantam, M. L.; Raghavan, K. V. *J. Am. Chem. Soc.* **2001**, *123*, 9220; (b) Choudary, B. M.; Chowdari, N. S.; Jyothi, K.; Kantam, M. L. *J. Am. Chem. Soc.* **2002**, *124*, 5341.
5. (a) Song, C. E.; Jung, D.; Roh, E. J.; Lee, S.; Chi, D. Y. *Chem. Commun.* **2002**, 3038; (b) Branco, L. C.; Afonso, C. A. M. *Chem. Commun.* **2002**, 3036; (c) Branco, L. C.; Afonso, C. A. M. *J. Org. Chem.* **2004**, *69*, 4381.
6. Lee, D.; Lee, H.; Kim, S.; Yeom, C.-E.; Kim, B. M. *Adv. Synth. Catal.* **2006**, *348*, 1021.
7. Whitehead, D. C.; Travis, B. R.; Borhan, B. *Tetrahedron Lett.* **2006**, *47*, 3797.
8. Johnson, R. A. In *Catalytic asymmetric dihydroxylation discovery and development Catalytic Asymmetric Synthesis*; Ojima, I., Sharpless, K. B., Eds.; VCH: New York, 2000; pp 357–398.
9. Pappo, R.; Allen, D. S.; Lemieux, R. U.; Johnson, W. S. *J. Org. Chem.* **1956**, *21*, 478.
10. Somaiah, P. V.; Reddy, K. B.; Sethuram, B.; Rao, T. N. *Indian J. Chem., Sect A. EN* **1988**, *27*, 876.

11. When olefin cleavage was performed stilbene diol as the starting material under the same basic reaction conditions, only 75% of benzaldehyde was obtained after 24 hours.
12. Geng, X.-L.; Wang, Z.; Li, X.-Q.; Zhang, C. *J. Org. Chem.* **2005**, *70*, 9610.
13. Junttila, M. H.; Hormi, O. E. O. *J. Org. Chem.* **2004**, *69*, 4816.
14. (a) Hirano, M.; Yakabe, S.; Clark, J. H.; Kudo, H.; Morimoto, T. *Synth. Commun.* **1996**, *26*, 1875; (b) Hirano, M.; Yakabe, S.; Clark, J. H.; Morimoto, T. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2693.
15. Zhao, M.; Li, J.; Mano, E.; Song, Z.; Tschaen, D. M.; Grabowski, E. J. J.; Reider, P. *J. Org. Chem.* **1999**, *64*, 2564.
16. Besemer, A. D. European Patent 1341717, 2004.
17. (a) Carlsen, H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936; (b) Rossiter, B. E.; Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 464.
18. *A general procedure for the olefin cleavage and treatment for osmium recycle*: A solution of $NaIO_4$ (0.5 mmol) and $NaClO_2$ (2.0 mmol) in water (5 mL) was added to a solution containing olefin (1.0 mmol) in acetonitrile (5 mL). To the resulting suspension was added 4 wt % aq solution of osmium tetroxide (0.01 mmol, 61 μL), and the mixture was stirred at the room temperature for 14 h. Then 150 mol % of isopropyl alcohol (115 μL) and potassium hydroxide (98 mg) were added to the reaction mixture and the mixture was stirred for another 8 h. Organic products were extracted with TBME (6 mL × 3) and the combined organic layer was dried (anhyd $MgSO_4$). Before running a new reaction cycle, the remaining aqueous layer was neutralized to pH 6–7 by adding 1 N HCl (0.5–0.8 mL) and stirring for 10 min. Then a new substrate (1.0 mmol), $NaIO_4$ (0.5 mmol), $NaClO_2$ (2.0 mmol) and acetonitrile (5 mL) were added, and the mixture was stirred for 14 h as the second run of the reaction. The extracted residue was dried with anhyd $MgSO_{4,}$ and filtered. The organic solution was directly analyzed with HPLC after addition of an internal standard or purified by flash column chromatography to yield the desired product.